UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte WILLIAM J. MCBRIDE and GARY L. GRIFFITHS

Appeal No. 2005-2026
Application No. 09/676,783

ON BRIEF

Before SCHEINER, GRIMES and GREEN, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 24-43, all the claims remaining in the application.

BACKGROUND

> Radiolabeled peptides are useful in the diagnosis and therapy of a variety of human disease states that are characterized by overexpression of peptide hormone receptors . . . [F]or example, it has been shown that radiolabeled analogues of LHRH (luteinizing hormone releasing hormone) and somatostatin selectively bind to hormone-sensitive tumors characterized by cell-surface overexpression of LHRH hormone receptors. Similarly, peptide hormone analogues such as ^{123}I-vasoactive intestinal peptide (VIP), ^{99m}Tc-P829, ^{111}In-DTPA Octreotide and ^{111}In-bisMSH-DTPA have been used to image human tumors that over express VIP, somatostatin, somatostatin and melanocyte stimulating hormone (MSH) receptors respectively.

Specification, page 1.

Various methods of radiolabeling peptides are known, each with certain disadvantages. For example, "[m]any tyrosine-containing peptides may be labeled with

[radioiodine]" (id., page 2), however, "^{123}I, the most useful isotope in vivo, is very expensive . . . must be produced in a cyclotron . . . [and] has a half-life of only 13.2 hours" (id.). "^{99m}Tc and ^{188}Re are preferred for diagnostic and therapeutic uses, respectively" (id.) and "[s]ome peptides either directly contain, or are amenable to the introduction of, residues that allow direct binding of . . . ^{99m}Tc and ^{188}Re to the peptide . . . Complexes of this type tend, however, to be heterogeneous and unstable, which limits their clinical utility . . . [and] direct binding of the metal to an amino acid side chain can greatly influence the peptide conformation, thereby deleteriously altering [its] receptor binding properties" (id., pages 2-3).

"Most peptides either do not contain a metal-binding amino acid sequence motif or . . . are not amenable to suitable sequence modifications that would permit introduction of such a motif. Some means of rendering the peptide capable of binding radiometals must therefore be introduced into the peptide" (id., page 3). "Chelates have conventionally been attached via covalent linkages to the N-terminus of a peptide or peptide analogue, following independent synthesis of the peptide and chelate moieties[,]" but "[c]oupling in this manner is . . . undesirable when the N-terminus of the peptide plays an important role in its receptor binding properties" (id.). "Alternatively, chelating agents have been introduced into peptide side chains by . . . site-selective reactions involving particular amino acid residues . . . [but] [t]his method is inherently limited by the lack of chemical selectivity available when more than one side chain can potentially react with the chelator, or when the peptide sequence does not contain an amino acid that can be derivatized in this way . . . [W]hen multidentate ligands are used[,] [a] single ligand molecule can react with multiple peptide molecules resulting in . . . cross-linked products" (id., pages 3-4).

The present invention is directed to treating tumors with radiolabeled radiometal-binding peptide analogues "prepared by site-specifically introducing [ ] metal-chelating moieties into peptides . . . synthesized by solid-phase or solution-phase methods" (id., page 10)

> using differentially protected bis-amino acid derivatives in which either amino function can be selectively deprotected. These derivatives are introduced into a growing peptide chain during peptide synthesis by conventional peptide coupling methodology. One of the amino functions is then selectively deprotected, allowing subsequent coupling of either all or a part of a chelating molecule, or addition of further amino acid residues to continue the peptide synthesis. Peptide synthesis can be continued by coupling at the α-amino group, leading to a peptide with a conventional amide backbone, or at the side-chain amino group to produce a peptide whose amide backbone is interrupted by the side chain structure. Alternatively, the free amino function can be used to cyclize onto a reactive functionality located elsewhere in the peptide . . . The chelating moiety may be added as a complete unit, in protected or unprotected form, or may be synthesized in stepwise fashion to construct the complete chelating structure. Id., page 12.

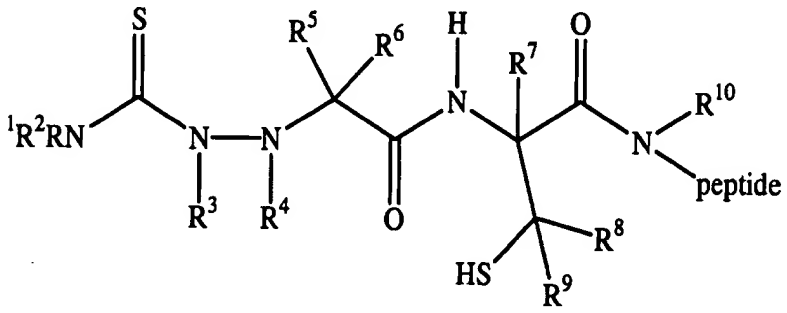
This approach "allows the placement of a radiometal-binding moiety anywhere in a peptide sequence" (id., page 15), "while retaining the [peptide's] ability to specifically bind" its target (id., page 6).

> Peptides according to the invention include . . . cyclic metal-binding analogues of LHRH, vasoactive intestinal peptide (VIP), heregulins (*erbB* binding peptides) α, β1, β2, and β3, melanotropin (α-MSH), somatostatin, calcitonin, epidermal growth factor, gonadotrophin releasing hormone, heregulins growth hormone releasing hormone, dynorphin, calcitonin gene-related peptide, vasotocin, mesotonin, adrenocorticotropic hormone, corticotropin, gonadotropin, prolactin, vasopressin, oxytocin, substance P, substance K, and angiotensin.

Specification, page 10.

Independent claim 24, directed to a method of treating a tumor by administering a radiolabeled radiometal-binding peptide analogue, is representative of the subject matter on appeal:

24. A method of treating a tumor, comprising administering to a human patient a radiolabeled peptide and a pharmaceutically acceptable carrier, wherein said peptide comprises a radiometal-binding moiety comprising the structure:



wherein R^1, R^2, and R^3 independently are selected from the group consisting of H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_3-C_6 cycloalkyl, substituted C_3-C_6 cycloalkyl, heterocycloalkyl, C_6-C_{12} aryl, C_6-C_{12} substituted aryl, heteroaryl, substituted heteroaryl, alkaryl, and a protecting group, provided that at least one of R^1, R^2, or R^3 is H,

R^5, R^7, R^8, R^9 and R^{10} independently are selected from the group consisting of H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_6-C_{12} aryl, and substituted C_6-C_{12} aryl, and R^8 and R^9 together or R^7 and R^9 together may form a cycloalkyl or substituted cycloalkyl ring,

R^4 and R^6 together form a direct bond or are independently selected from the group consisting of C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_6-C_{12} aryl, and substituted C_6-C_{12} aryl, and wherein NR^{10} is located at the N-terminus of said peptide, or is located on an amino acid side chain of said peptide.

DISCUSSION

Claims 24 through 43 stand rejected under the first paragraph of 35 U.S.C. § 112, as failing "to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Answer, page 4).

"The 'written description' requirement serves a teaching function, . . . in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.'" University of Rochester v. G.D. Searle & Co., Inc., 358 F.3d 916, 922, 69 USPQ2d 1886, 1891 (Fed. Cir. 2004) (citation omitted). Another "purpose of the 'written description' requirement is . . . [to] convey with reasonable clarity to those skilled in the art that, as of the filing date [ ], [the applicant] was in possession of the invention." Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See also Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d 1316, 1329, 63 USPQ2d 1609, 1617 (Fed. Cir. 2002).

"[A]pplicants have some flexibility in the 'mode selected for compliance' with the written description requirement" (University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896); it is well settled that actual reduction to practice is not necessary to satisfy the requirement (id., at 926, 69 USPQ2d at 1894). The requirement is satisfied when the specification "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." University of Rochester, 358 F.3d at 928, 69 USPQ2d at 1896. Whether or not a specification satisfies the requirement is a question of fact, which must be resolved on a case-by-case basis (Vas-Cath, 935 F.2d at 1562-63, 19 USPQ2d at 1116), and it is the examiner's "initial burden [to] present[ ] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)).

The USPTO has summarized a number of factors to be considered in making this determination; they include "the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention." Guidelines for Examination of Patent applications Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001). "Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." Id.

As discussed above, the claims are directed to a method of treating a tumor by administering a radiometal-binding peptide analogue in a pharmaceutical carrier. A schematic diagram of the radiometal-binding peptide analogue is shown in independent claim 24 – with the exception of claim 41, none of the claims specifies the peptide portion of the analogue. The examiner has focused exclusively on the peptide portion of the analogue in arguing that "[t]here is not enough description in the specification as to the different kind of tumor(s), peptides, modes of administration, dosage and test procedures or steps in specific terms as to the treatment method" "to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Answer, page 4). The examiner argues that the specification "teaches a specific method of radiolabelling the peptide and a general in vitro assay method" and "[i]t is not apparent from the general in vitro assay method, the specific qualifying feature, if any, of the binding effect that translates into a therapeutic effect, absent any experimental results" (id., page 6).

In our view, the examiner's focus on the peptide portion of the radiometal-binding peptide analogue is misplaced. As explained in the specification, the peptide moiety of the analogue serves to carry or direct a radiometal (bound by the radiometal-binding moiety) to a target antigen on a tumor (Specification, page 1), while "[t]he radioactivity of the radio[metal] allows . . . treatment of the tumor" (id., page 15). In keeping with this, appellants submitted a number of journal articles "demonstrat[ing] that, at the time the application was filed, it was known that peptides related to those [disclosed] in the present application [were] promising in vitro candidates for the treatment of certain tumors . . . [and] that the in vitro results could be extrapolated to the use of such peptides in radionuclide therapy to treat certain tumors in vivo" (Brief, page 4).

Appellants' position is essentially that the presently claimed "method of treating tumors [is] based upon the discovery of a new method of radiolabeling peptides" (Reply Brief, page 5); that many tumor-specific peptides are described in the specification; that methods of using these and other radiolabeled tumor-specific peptides to target and treat tumors would have been known to those skilled in the art at the time of the invention; and that those skilled in the art would have recognized that appellants had possession of a method of treating tumors using a genus of radiometal-binding peptide analogues at the time of filing.

We agree with appellants that their disclosure, considered in combination with the level of skill and knowledge in the art, conveys with reasonable clarity that appellants were in possession of the claimed invention as of their effective filing date. We find that the examiner's initial burden of establishing that one skilled in the art would not have recognized that appellants were in possession of what is claimed has not been met. Accordingly, the rejection is reversed.

REVERSED

Toni R. Scheiner
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

Lora M. Green
Administrative Patent Judge

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